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1. A substantially pure preparation of a cell cycle regulatory (CCR) protein, or a fragment thereof, which specifically binds to a cyclin-dependent kinase (CDK), the full-length form of said CCR-protein having an approximate molecular weight in the range of 14.5kD to 16kD.
  2. The CCR-protein of claim 1, comprising an amino acid sequence at least 60% homologous to an amino acid sequence represented in SEQ ID No. 2.
  3. The CCR-protein of claim 1, comprising an amino acid sequence at least 60% homologous to an amino acid sequence represented in SEQ ID No. 4.
  4. The CCR-protein of claim 1, including an amino acid sequence represented by the general formula:

Met-Met-Met-Gly-Xaa-Xaa-Xaa-Val-Ala-Xaa-Leu-Leu-Leu-  
Xaa-Xaa-Gly-Ala-Xaa-Xaa-Asn-Cys-Xaa-Asp-Pro-Xaa-Thr-  
Xaa-Xaa-Xaa-Arg-Pro-Val-His-Asp-Ala-Ala-Arg-Glu-Gly-  
Phe-Leu-Asp-Thr-Leu-Val-Val-Leu-His-Xaa-Xaa-Gly-Ala-  
Arg-Leu-Asp-Val-Arg-Asp-Ala-Trp-Gly-Arg-Leu-Pro-Xaa-  
Asp-Leu-Ala-Xaa-Glu-Xaa-Gly-His-Xaa-Asp-Xaa-Xaa-Xaa-  
Tyr-Leu-Arg-Xaa-Ala-Xaa-Gly.

5. The CCR-protein of claim 1, which CCR-protein functions in one of either role of an agonist of cell-cycle regulation or an antagonist of cell-cycle regulation.
6. A substantially pure preparation of a p15 polypeptide, or a fragment thereof, having an amino acid sequence at least 60% homologous to SEQ ID No. 4.
7. The polypeptide of claim 6, which specifically binds a cyclin dependent kinase (CDK).
8. The polypeptide of claim 6, including an amino acid sequence represented by the general formula:

Met-Met-Met-Gly-Xaa-Xaa-Xaa-Val-Ala-Xaa-Leu-Leu-Leu-  
Xaa-Xaa-Gly-Ala-Xaa-Xaa-Asn-Cys-Xaa-Asp-Pro-Xaa-Thr-  
Xaa-Xaa-Xaa-Arg-Pro-Val-His-Asp-Ala-Ala-Arg-Glu-Gly-  
Phe-Leu-Asp-Thr-Leu-Val-Val-Leu-His-Xaa-Xaa-Gly-Ala-  
Arg-Leu-Asp-Val-Arg-Asp-Ala-Trp-Gly-Arg-Leu-Pro-Xaa-  
Asp-Leu-Ala-Xaa-Glu-Xaa-Gly-His-Xaa-Asp-Xaa-Xaa-Xaa-  
Tyr-Leu-Arg-Xaa-Ala-Xaa-Gly.

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9. The polypeptide of claim 6, wherein said polypeptide which functions in one of either role of an agonist of cell cycle regulation or an antagonist of cell cycle regulation.
10. An immunogen comprising the CCR-protein of claim 1, in an immunogenic preparation, said immunogen being capable of eliciting an immune response specific for said CCR-protein.

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11. An antibody preparation specifically reactive with an epitope of the immunogen of claim 10.

12. An immunogen comprising the polypeptide of claim 6 in an immunogenic preparation, said immunogen being capable of eliciting antibodies specific for said p15 polypeptide.

13. An antibody preparation specifically reactive with an epitope of the immunogen of claim 12.

14. A recombinant p15 polypeptide, or a fragment thereof, having an amino acid sequence at least 60% homologous to SEQ ID No. 4.

15. The polypeptide of claim 14, which p15 polypeptide functions in one of either role of an agonist of cell cycle regulation or an antagonist of cell cycle regulation.

16. The polypeptide of claim 14, which p15 polypeptide binds to a cyclin dependent kinase.

17. The polypeptide of claim 14, comprising an amino acid sequence represented by the general formula:

Met-Arg-Glu-Glu-Asn-Lys-Gly-Met-Pro-Ser-Gly-Gly-Gly-Ser-  
Asp-Glu-Gly-Leu-Ala-Thr-Pro-Ala-Arg-Gly-Leu-Val-Glu-Lys-  
Val-Arg-His-Ser-Trp-Glu-Ala-Gly-Ala-Asp-Pro-Asn-Gly-Val-  
Asn-Arg-Phe-Gly-Arg-Arg-Ala-Ile-Gln-Val-Met-Met-Met-Gly-  
Xaa-Xaa-Xaa-Val-Ala-Xaa-Leu-Leu-Leu-Xaa-Xaa-Gly-Ala-Xaa-  
Xaa-Asn-Cys-Xaa-Asp-Pro-Xaa-Thr-Xaa-Xaa-Xaa-Arg-Pro-Val-  
His-Asp-Ala-Ala-Arg-Glu-Gly-Phe-Leu-Asp-Thr-Leu-Val-Val-  
Leu-His-Xaa-Xaa-Gly-Ala-Arg-Leu-Asp-Val-Arg-Asp-Ala-Trp-  
Gly-Arg-Leu-Pro-Xaa-Asp-Leu-Ala-Xaa-Glu-Xaa-Gly-His-Xaa-  
Asp-Xaa-Xaa-Xaa-Tyr-Leu-Arg-Xaa-Ala-Xaa-Gly-Asp

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18. The polypeptide of claim 14, wherein said polypeptide is cloned from a human cell.
19. The polypeptide of claim 14, wherein said polypeptide is a fusion protein further comprising, a second polypeptide portion having an amino acid sequence from a protein unrelated the protein of SEQ ID No. 4.
20. The polypeptide of claim 19, wherein said fusion protein is functional in a two-hybrid assay.
21. A substantially pure nucleic acid having a nucleotide sequence which encodes a cell cycle regulatory (CCR) protein, or a fragment thereof, which specifically binds a cyclin-dependent kinase (CDK), the full-length form of said CCR-protein having an approximate molecular weight in the range of 14.5kD to 16kD.
22. The nucleic acid of claim 21, wherein said CCR-protein encoded by said nucleotide sequence has an amino acid sequence at least 60% homologous to an amino acid sequence represented in SEQ ID No. 2.
23. The nucleic acid of claim 21, wherein said CCR-protein encoded by said nucleotide sequence has an amino acid sequence at least 60% homologous to an amino acid sequence represented in SEQ ID No. 4.
24. The nucleic acid of claim 21, wherein said CCR-protein encoded by said nucleotide sequence has an amino acid sequence represented by the general formula:  
  
Met-Met-Met-Gly-Xaa-Xaa-Xaa-Val-Ala-Xaa-Leu-Leu-Leu-  
Xaa-Xaa-Gly-Ala-Xaa-Xaa-Asn-Cys-Xaa-Asp-Pro-Xaa-Thr-  
Xaa-Xaa-Xaa-Arg-Pro-Val-His-Asp-Ala-Ala-Arg-Glu-Gly-  
Phe-Leu-Asp-Thr-Leu-Val-Val-Leu-His-Xaa-Xaa-Gly-Ala-  
Arg-Leu-Asp-Val-Arg-Asp-Ala-Trp-Gly-Arg-Leu-Pro-Xaa-  
Asp-Leu-Ala-Xaa-Glu-Xaa-Gly-His-Xaa-Asp-Xaa-Xaa-Xaa-  
Tyr-Leu-Arg-Xaa-Ala-Xaa-Gly.
25. The nucleic acid of claim 21, wherein said CCR-protein encoded by said nucleotide sequence functions in one of either role of an agonist of cell cycle regulation or an antagonist of cell cycle regulation.
26. The nucleic acid of claim 21, wherein said nucleotide sequence hybridizes under stringent conditions to a nucleic acid probe corresponding to at least 12 consecutive nucleotides of either of SEQ ID No. 1 or SEQ ID No. 2.

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27. The nucleic acid of claim 21, further comprising a transcriptional regulatory sequence operably linked to said nucleotide sequence so as to render said nucleic acid suitable for use as an expression vector.
28. An expression vector, capable of replicating in at least one of a prokaryotic cell and eukaryotic cell, comprising the nucleic acid of claim 21.
29. A host cell transfected with the expression vector of claim 28 and expressing said polypeptide.
30. A method of producing a recombinant cell-cycle regulatory (CCR) protein comprising culturing the cell of claim 29 in a cell culture medium to express said CCR-protein and isolating said CCR-protein from said cell culture.
31. A transgenic animal having cells which harbor a transgene comprising the nucleic acid of claim 21.
32. A transgenic animal in which expression of a CCR-protein is disrupted in one or more tissue of said animal.
33. A recombinant gene comprising a nucleotide sequence at least 60% homologous to either of SEQ ID No. 1 or SEQ ID No.3, or a fragment thereof, said nucleotide sequence operably linked to a transcriptional regulatory sequence in an open reading frame and translatable to a polypeptide capable of functioning in one of either role of an agonist of cell cycle regulation or an antagonist of cell cycle regulation.
34. The recombinant gene of claim 33, which is derived from a cDNA clone.
35. The recombinant gene of claim 33, which is derived from a genomic clone and optionally includes intronic nucleotide sequences disrupting said open reading frame.
36. The recombinant gene of claim 33, wherein said polypeptide is a fusion protein derived from at least two unrelated proteins, one of which includes a CDK-binding portion of SEQ ID No. 2 or SEQ ID No. 4.

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37. An animal model for studying cellular disorders comprising a non-human animal in which at least one allele of a gene encoding a protein represented by SEQ ID No. 4 is mutated or mis-expressed.
38. A probe/primer comprising a substantially purified oligonucleotide, said oligonucleotide containing a region of nucleotide sequence which hybridizes under stringent conditions to at least 10 consecutive nucleotides of sense or antisense sequence of SEQ ID No. 1 or SEQ ID No. 3, or naturally occurring mutants thereof.
39. The probe/primer of claim 38, further comprising a label group attached thereto and able to be detected.
40. A diagnostic test kit for identifying a transformed cell, comprising the probe/primer of claim 38, for measuring a level of nucleic acid encoding a cell-cycle regulatory protein in a sample of cells isolated from a patient.
41. A diagnostic test kit for identifying transformed cells, comprising an antibody specific for a p15 protein for measuring, in a sample of cells isolated from a patient, a level of said p15 protein.
42. A method of treating an animal having unwanted cell growth characterized by a loss of function of a cell-cycle regulatory (CCR) protein, comprising administering a therapeutically effective amount of an agent able to inhibit a kinase activity of a G<sub>1</sub> phase cyclin dependent kinase (CDK).
43. The method of claim 42, comprising administering a nucleic acid construct encoding a CCR-protein, or fragment thereof, under conditions wherein said construct is incorporated by CCR-deficient cells and the CCR-protein is expressed.
44. The method of claim 43, wherein said CCR-protein comprises an amino acid sequence represented by the general formula:

Met-Met-Met-Gly-Xaa-Xaa-Xaa-Val-Ala-Xaa-Leu-Leu-Leu-  
Xaa-Xaa-Gly-Ala-Xaa-Xaa-Asn-Cys-Xaa-Asp-Pro-Xaa-Thr-  
Xaa-Xaa-Xaa-Arg-Pro-Val-His-Asp-Ala-Ala-Arg-Glu-Gly-  
Phe-Leu-Asp-Thr-Leu-Val-Val-Leu-His-Xaa-Xaa-Gly-Ala-  
Arg-Leu-Asp-Val-Arg-Asp-Ala-Trp-Gly-Arg-Leu-Pro-Xaa-  
Asp-Leu-Ala-Xaa-Glu-Xaa-Gly-His-Xaa-Asp-Xaa-Xaa-Xaa-  
Tyr-Leu-Arg-Xaa-Ala-Xaa-Gly.

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45. The method of claim 43, wherein said CCR-protein comprises an amino acid sequence at least 60% homologous to an amino acid sequence represented in one of SEQ ID Nos. 2, 4 or 6.
46. The method of claim 42, comprising administering a peptidomimetic of a cell-cycle regulatory protein which binds to and inhibits the G<sub>1</sub> phase CDK.
47. A method of treating an animal having unwanted cell growth characterized by a loss of responsiveness of a population of cells to a transforming growth factor (TGF) protein, comprising administering a therapeutically effective amount of an agent able to inhibit a kinase activity of a G<sub>1</sub> phase cyclin dependent kinase (CDK).
48. The method of claim 47, comprising administering therapeutic amount of a CDK inhibitor selected from the group consisting of:

- (i) a nucleic acid construct encoding a cell-cycle regulatory protein represented by the general formula

Met-Met-Met-Gly-Xaa-Xaa-Xaa-Val-Ala-Xaa-Leu-  
Leu-Leu-Xaa-Xaa-Gly-Ala-Xaa-Xaa-Asn-Cys-Xaa-  
Asp-Pro-Xaa-Thr-Xaa-Xaa-Xaa-Arg-Pro-Val-His-  
Asp-Ala-Ala-Arg-Glu-Gly-Phe-Leu-Asp-Thr-Leu-  
Val-Val-Leu-His-Xaa-Xaa-Gly-Ala-Arg-Leu-Asp-  
Val-Arg-Asp-Ala-Trp-Gly-Arg-Leu-Pro-Xaa-Asp-  
Leu-Ala-Xaa-Glu-Xaa-Gly-His-Xaa-Asp-Xaa-Xaa-  
Xaa-Tyr-Leu-Arg-Xaa-Ala-Xaa-Gly;

- (ii) a nucleic acid construct encoding a cell-cycle regulatory protein comprising an amino acid sequence at least 60% homologous to an amino acid sequence represented in one of SEQ ID Nos. 2, 4 or 6; and
- (iii) a peptidomimetic of the cell-cycle regulatory protein of (a) or (b), which peptidomimetic binds to and inhibits the CDK.
49. A recombinant transfection system, comprising
- (i) a gene construct encoding a cell-cycle regulatory (CCR) protein and operably linked to a transcriptional regulatory sequence for causing expression of the CCR-protein in eukaryotic cells, the CCR-protein being characterized by an ability to bind to inhibit activation of cyclin dependent kinase, and
- (ii) a gene delivery composition for delivering the gene construct to a cell and causing the cell to be transfected with said gene construct.

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50. The recombinant transfection system of claim 52, wherein the gene delivery composition is selected from a group consisting of a recombinant viral particle, a liposome, and a poly-cationic nucleic acid binding agent,
51. A method of determining if a subject is at risk for a disorder characterized by unwanted cell proliferation, comprising detecting, in a tissue of said subject, the presence or absence of a genetic lesion characterized by at least one of  
a mutation of a gene encoding a protein represented by SEQ ID No. 4, or a homolog thereof; and the mis-expression of said gene.
52. The method of claim 51, wherein detecting said genetic lesion comprises ascertaining the existence of at least one of  
i. a deletion of one or more nucleotides from said gene,  
ii. an addition of one or more nucleotides to said gene,  
iii. an substitution of one or more nucleotides of said gene,  
iv. a gross chromosomal rearrangement of said gene.  
v. a gross alteration in the level of a messenger RNA transcript of said gene,  
vi. the presence of a non-wild type splicing pattern of a messenger RNA transcript of said gene, and  
vii. a non-wild type level of said protein.
53. The method of claim 51, wherein detecting said genetic lesion comprises  
i. providing a probe/primer comprising an oligonucleotide containing a region of nucleotide sequence which hybridizes to a sense or antisense sequence of SEQ ID No. 3 or naturally occurring mutants thereof or 5' or 3' flanking sequences naturally associated with said gene;  
ii. exposing said probe/primer to nucleic acid of said tissue; and  
iii. detecting, by hybridization of said probe/primer to said nucleic acid, the presence or absence of said genetic lesion.
54. The method of claim 53, wherein detecting said lesion comprises utilizing said probe/primer to in a polymerase chain reaction (PCR).
55. The method of claim 53, wherein detecting said lesion comprises utilizing said probe/primer in a ligation chain reaction (LCR).

56. The method of claim 52, wherein the level of said protein is detected in an immunoassay.
57. A method of determining a risk of cellular transformation of a cell, comprising detecting in the cell the presence of a protein complex between cyclin dependent kinase (CDK) and a p15 protein having an amino acid sequence represented by SEQ ID No. 4, or a homolog thereof.

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